Division of Microbiology
and Infectious Diseases

SOURCE DOCUMENTATION STANDARDS

For
DMID Clinical Studies

Version 2.0 March 16, 2004

National Institute of Allergy and Infectious Diseases
National Institutes of Health
Department of Health and Human Services

DMID/NIAID
DMID Source Documentation Standards (Version 2.0 March 16, 2004)

The Division of Microbiology and Infectious Diseases (DMID), National Institute of Allergy and Infectious Diseases (NIAID), and National Institutes of Health (NIH) supports a large number of clinical studies and trials through both contract and grant mechanisms. This Standard is provided to aid DMID supported investigators and research personnel in establishing a system of records.

This Standard has been assembled by using the International Conference on Harmonisation (ICH) Good Clinical Practices (GCP) Guidelines (E6), the Code of Federal Regulations (CFR), and guidances that apply to the involvement of human subjects in clinical research. It is applicable to all DMID funded clinical trial sites conducting studies on human subjects, both domestic and international.

ICH GCP 1.51 defines Source Data as "All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies)."

ICH GCP 1.52 defines Source Documents as "Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subject diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial)."

Documentation of source data is necessary for the reconstruction, evaluation, and validation of clinical findings, observations, and other activities during a clinical trial. Source documentation serves to substantiate the integrity of trial data, confirm observations that are recorded, and confirm the existence of subjects. This standard also serves to ensure data quality by creating audit trails and enabling verification that data are present, complete, and accurate. DMID studies will be monitored using these standards.

Sites that are participating in multicenter or industry-sponsored IND trials should consult their Manual of Procedures and/or source document workbooks for specific instruction and forms. Study-specific source documentation workbooks may be provided by the study management in a multicenter trial.

Local, state, institution, institutional review board (IRB)/independent ethics committee (IEC) policies and procedures may be different from those stated in this standard. Always refer to local, state, institution, IRB/IEC policies and procedures and follow them if they are more stringent than the DMID Standards.

According to the ICH GCP 4.9: "The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports. Data reported on the Case Report Forms, which are derived from source documents, should be consistent with the source documents or discrepancies should be explained." For more information on these guidelines and documentation requirements, please reference the DMID GCP handbook (http://www.niaid.nih.gov/dmid/clinresearch) or the websites for ICH and FDA (www.ich.org and www.fda.gov). Search engines will take you to various regulations and the GCP guidelines. DMID requires adherence to GCP standards for all studies sponsored by the Division.

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Topic	Source Documentation Methods/Procedures	Adequacy Criteria
Addenda, to source documentation (SD) See also Documentation Standards; Inadequate Source Documentation; and Error Corrections.	**Recommended, when applicable:** When SD is found to be incomplete (whether by site staff during internal QA, or a monitor during a site visit), the circumstances of the deficiency may be documented in a Chart Note dated and situated in real-time in the study subject's SD. The entry should be made by a clinician presently responsible for the study subject. If "missing" SD is obtained at a later date, its incorporation into the research record may be acknowledged in a Chart Note dated and situated in real-time in the study subject's SD. The entry should likewise be made by the clinician presently responsible for the study subject.	Sites must not modify past-dated research records in an attempt to resolve SD deficiencies noted during internal QA or a site monitoring visit. Altering past-dated records without appropriately dating the new entry in real-time is strongly discouraged because such entries may be considered unverifiable and potentially fraudulent. Refer to proper procedures for making addenda to SD, at left. See also Error Corrections.
Case Report Forms (not used as Source Documentation)	Contains PID (participant/patient identifier, study identifier) and trial data. No personal identifiers (e.g., name, initials, SSN, exact date of birth) should be entered on the Case Report Form. Year of birth is okay. For studies where exact personal identifiers are crucial, i.e. date of birth, discuss first with the Office of Regulatory Affairs, DMID. Also see Subject Specific Information.	
Case Report Forms, used as Source Documentation	**Required:** Per ICH E6 Guidelines for Good Clinical Practice 6.4.9, trial design must identify any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data), and considered to be source data. **DMID Allowable Methods:** • CRFs to be used as SDs must be identified in the Protocol, MOP, or SD agreement/statement before the study begins. • Use an original completed CRF (or photocopy/NCR copy of a completed CRF) as the SD. The original CRF must be signed, credentialed, and dated. The CRF must be designed to capture raw data. **NOTE: Any changes/error corrections subsequently made to the original CRF must be carried over to the copy and vice-versa. NCR copies sent to another location, e.g., a lab, should also be copied to the study subject's source documentation record.** • Sites may be allowed to design their own Study Subject Encounter Forms/SD Workbook, or flowsheets that correspond to data items on CRFs. Such forms should allow for free-form entries (akin to Chart Notes) to allow clinicians to record any observations pertinent to the study subject's clinical status. Completed Study Subject Encounter Forms/SD Workbooks or flowsheets that will be used as SD must be signed, credentialed, and dated by the clinician responsible for their completion. See also Flowsheets. • Additional SD may still be required to maintain "adequate and accurate case histories" that reflect all pertinent aspects of study subjects' clinical status during given time periods. The decision to allow a particular type of completed CRF to be used in establishing source documentation (and the particulars of how such forms may be used) rests with the Research Sponsor, DMID.	
Chart Note, clinician (Progress Note or Clinic Note)	**Required:** All original Chart Notes must be signed, credentialed, and dated by the clinician responsible for their creation. **Recommended:** It is strongly recommended that all Chart Notes and other source documentation be kept in either forward or reverse order by date to support the chronology of study subject events.	
Chemistries	See Lab tests, Routine, specimen collection and results.	

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Communications, verbal	**Required (one of the following):** • Chart Note • Contact report (i.e., written documentation of conversation that is signed, credentialed, and dated, then maintained in a study subject's SD)	Verification of (or attempts to verify) study subject diagnoses or events via telephone call to outside clinicians should be documented in a study subject's SD by means of contact reports.
Communications, written	**Required (one of the following):** • Original letters/documents, or copies of same	Correspondence must include appropriate study subject identifier(s) so monitor can verify that documents correspond to particular study subjects.
Compliance, study product (if required by Protocol)	**Required (one of the following):** • Chart Note, • Study Subject Encounter Form, • Study Subject Diary, or • CRF used as SD	For CRFs requiring specific information on study subject product compliance, a corresponding Chart Note, entry in a Study Subject Encounter Form, entry in study subject diary, or CRF used as SD should reflect the percentages or numbers of missed doses (or vaccinations) and/or other relevant information. [For drug studies, if no drug is returned for a Protocol-required pill count, the SD must so indicate.]
Confidentiality, study subject	**Required:** All source documents must be consistently labeled with appropriate PIDs (Participant Identification Numbers). At the start of the study it should be determined what will be source. The source documents must contain adequate information to link back to the subject in order to confirm the identity of the subject. Source documents that are also case report forms must only contain a PID that will link back to the subjects. A separate list or participant information forms that link PIDs to actual individuals must be maintained. These information/contact forms must not be sent or transmitted to the data center or other entities. These contract/information forms are source documents belonging to the site. The source documents must provide adequate documentation so that the monitor is able to verify that documents correspond to particular study subjects. **Training Point** The Code of Federal Regulations (21 CFR 50.25; 45CFR46.116(a)(5)) requires that study subjects be informed of the extent, if any, to which confidentiality of records identifying the study subject will be maintained. In DMID-sponsored trials, through the informed consent process, study subjects are assured that their records will be maintained confidentially to the extent permitted by law; that they will be identified by code (PID); that personal information will not be released without study subjects' written permission; and that they will not be personally identified in any publication about the study. They are also informed that their records may be reviewed, under guidelines of the Federal Privacy Act, by the FDA, the National Institute of Allergy and Infectious Diseases/DMID, the study monitors, and the pharmaceutical company(ies) which supply the study treatment(s).	
Contact Reports	See Communications, verbal.	
Consent, study subject informed	See Informed Consent and Informed Consent requirements prior to study enrollment.	

Topic	Source Documentation Methods/Procedures	Adequacy Criteria
Consult Notes	**Required:** Consult note (Chart Note, or other typed/written summary inserted into study subject's SD file), signed, credentialed, and dated by responsible clinician.	Consult notes must include appropriate study subject identifier(s) so monitor can verify that documents correspond to particular study subjects.
Contraception, current method of birth control, Protocol-required counseling	**Required (one of the following):** • Pre-randomization/Screening Chart Note, • Completed Eligibility Checklist, or • CRF used as SD	Protocol-specific and/or IRB-required study subject counseling on requirements for use of appropriate contraception and current method of birth control must be documented in a Pre-randomization/Screening Chart Note, in addition to the signed Informed Consent form which acknowledges any such requirements. See criteria for Chart Note, clinician. In lieu of a Chart Note, the site may include an item on a signed, credentialed, and dated Eligibility Checklist or CRF to document that such counseling has occurred and to document current method of birth control. The checklist should correspond to the Protocol version approved by the local IRB at the time of the study subject's enrollment. See Entry Criteria.
Copies: Certified See also Electronic Medical Records.	**Required:** Certified Copy means a copy of original information that has been verified, as indicated by dated signature, as an exact copy having all of the same attributes and information as the original. A copy used as a source document must be certified that it was verified to be an exact copy of the original. • This provides an audit trail in the event that the copy appears to have been altered. • If the original document is retained elsewhere on-site/within the institution, the copy DOES need to be certified. There should be an identifier on the document indicating where the document originated from in the institution, i.e., the name of the department in the institution. • Monitors and FDA auditors may request to see the original documents or certified copies to verify validity of data for trial-related monitoring. • Documentation received via fax is NOT considered to be original, and must be certified. **DMID Allowable Methods:** Certification of a copy may be indicated by any of the following methods: • A signed or initialed and dated statement on the copy that indicates it is an exact copy of the original information. This is to be done by the person making the copy, or the person verifying that the copy is the same as the original. The statement may be in the form of a stamp, as long as it is accompanied by an original signature, or initials and date.	

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	• DMID prefers that outside institutions certify the copy prior to sending it. DMID realizes that this is not always possible. In cases where the sending institution does NOT certify the copy prior to sending it, the following will be acceptable: The receiving institution verifies that the copy is unaltered as received; a signed or initialed and dated statement on the copy indicates it is unaltered as received. This is to be done by the person receiving the copy. The statement may be in the form of a stamp, as long as it is accompanied by the original signature or initials of receiver and date. • Documents consisting of more than one page may be verified in a package as being one (1) copy, if the package of copies is to remain intact in the file. For verification, the first page of the copy must have on it a signed or initialed and dated statement/stamp that indicates the package consisting of X (specify) number of pages is an exact copy of the original information, or verification that it is unaltered as received. Each page must then be initialed and dated to verify that it is part of the package. **Training Point** These procedures are designed to maintain a continuous audit trail for clinical data from their source to their inclusion in the research record. All copies of outside records must contain adequate study subject identifiers for the monitor to verify that they correspond to a particular study subject. Monitors may occasionally request to see the original documents during routine monitoring to verify their existence; this does not mean that alterations or fraud are suspected. 21 CFR 11 FDA Guidance: E6 GCP, Section 1.51 FDA Guidance: Computerized Systems used in Clinical Trials (CSCT)	
Correspondence, study subject-specific	See Communications, written.	
Death	**Required (one of the following):** • Autopsy report, • Obituary, • Death certificate, or • Contact Report documenting verbal communication with physician or study subject family member or friend • Hospital discharge summary	An autopsy report, obituary, and/or death certificate may be included in a study subject's SD file for verification of the date and cause of death. It is also acceptable to document verbal communication with a physician or study subject family member/friend to substantiate the date and reported cause of death if official documents are not available.

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Deviations from Protocol (Formerly known as Protocol Violations and/or Protocol Deviations/ Departures)	**Required:** Protocol deviations occur when there is non-adherence to the Protocol and includes Informed Consent, Enrollment, and other occurrences of non-adherence to the Protocol. DMID does not allow any exemptions or eligibility criteria waivers for enrollment. These are enrollment deviations. Protocol deviations: • May result in a significant added risk to the study subject. • Occur when the subject or investigator has failed to adhere to significant Protocol requirements. • Occur when there is non-adherence to GCP • Occur when there is non-adherence to study procedures or schedules by either the subject or investigator, as specified by the Protocol. All deviations from a Protocol must be addressed in study subject SD. The documentation should include the reasons for the deviation and all attempts to prevent or correct them. For example, documentation of a missed visit would properly consist of a note explaining the missed visit and the site's attempts to locate the study subject to request that he/she come in to make up that visit. The site must complete a DMID Deviation Form documenting each Protocol deviation. The completed form must be sent to DMID unless specific instructions are provided by the study team or are included in the Protocol or Manual of Operations. If the IND sponsor is other than DMID, the form must also be sent to the sponsor according to their requirements. Protocol Deviation Forms should be sent to the local IRB/IEC per their guidelines. A completed copy of the DMID Protocol Deviation (PD) Form must be maintained in the Regulatory File as well as in the subject's source document. Copies of fax confirmation or e-mail printout confirming that PD Forms were submitted to DMID and the IND sponsor, if applicable, need to be included in the Regulatory File. DMID Recommended IRB reporting schedule: • Protocol deviations that result in increased risk to the study subject or affect subject eligibility to enroll in the study or continue in the study should be reported promptly to the IRB. • Protocol deviations affecting subject rights (e.g., informed consent issues) should be reported within 30 days of knowledge by the investigator. • Protocol deviations affecting the timing of reporting of safety information to the sponsor or IRB should be reported within 30 days of knowledge by the investigator. • Protocol deviations involving non-adherence to GCP or study procedures or schedules that have a material impact on the primary endpoints of the study should be reported within 60 days of knowledge or sooner, if required by IRB. • Protocol deviations that occur persistently and/or could impact the ability to properly analyze and interpret the data should be reported on at least a 90-day interval. • Protocol deviations that, in the opinion of the investigator and sponsor, have no material impact on the integrity of the study may be reported to the IRB annually, as part of the annual IRB review and re-approval process, and more frequently as specified by the IRB's internal procedures.	

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Discharge Summaries	See Communications, written.	
Documentation Standards	**Training Point** All research personnel should be aware of, and comply with, applicable standards for medical documentation as determined by their institutional policy, professional Code of Ethics, and licensing authority. General standards include: (1) maintain clinical records chronologically; (2) keep handwritten notes and signatures legible (if necessary, print one's name underneath the signature); (3) sign, credential, and date all entries; (4) make error corrections using accepted, obvious procedures; (5) never obliterate entries that require correction; (6) never destroy original documents if they require error correction; (7) keep study subject records secure, yet accessible; and (8) do not alter past-dated notes (e.g., by writing alongside or adding to prior entries). Research personnel include study-related staff. Inadequate source documentation by non-research personnel may be noted by the monitor but is not generally noted in site visit report unless: • It is a trend (i.e. numerous instances of incorrect error corrections). • If a clinic/Chart Note is not signed by the clinician, then the monitor cannot verify if it was research or non-research personnel who neglected to sign their note.	
Electronic Medical Records	The use of electronic medical records is acceptable in institutions that have adopted electronic medical records systems. If the institution has deemed the practice acceptable, then DMID will accept its usage in supporting documentation. Sites may either printout a copy of the medical record for the monitor's review or provide the monitor with access to an institutional computer to review the medical records online. For institutions with a policy prohibiting the monitor from accessing an institutional computer to review the medical records online, the site must provide a printed copy of the electronic medical record as described below: • Clinical Laboratory printouts ("print screens") retrieved from an institution's computer system are considered official representations of the source document and DO NOT need to be certified, signed, or dated. DMID will accept lab printouts if the institution laboratory name is part of the print out, and the subject's name (or study PID or patient identifier), date of test, and date of printout are included. If the lab printout does not include the institution laboratory name and date of printout, the site must document this information on the printout, and initial and date their entry. • Printouts of electronic medical records, retrieved from an institution's computer system are considered official representations of the source document and DO NOT need to be certified, signed, or dated. DMID will accept electronic medical record printouts if the institutional name is part of the print out, and the subject's name (or study PID or patient identifier), date of record, and date of printout are included. If the printout of the electronic medical record does not include the institutional name and date of printout, the site must document this information on the printout, and initial and date their entry. • In cases where the site must document information (institutional name and/or date of printout) on the electronic medical record or lab printout and the printout consists of more than one page, the package of printouts is to remain intact in the file. The first page of the printout must have on it the site's entry of missing identifying information, and the site staff's initials and date. The entry must indicate the number of pages included in the printout. Each page must then be initialed and dated to verify that it is part of the package.	
Electronic Signatures	The use of electronic signatures is acceptable in institutions that have adopted electronic medical records systems. If the institution has deemed the practice acceptable, then DMID will accept its usage in supporting source documentation.	
Eligibility Criteria	See Entry Criteria.	

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Endpoints, clinical or laboratory (if required by Protocol) See also Electronic Medical Records.	**Required (one of following, per Protocol or endpoint-specific CRF):** • Chart Note, • Consult Note, • CRF as SD, • Documentation of Death, • Radiology diagnostic interpretation, • Hard copy lab report with appropriate study subject identifier(s) and date of specimen collection, or • "Print Screen" copy of electronic lab report with appropriate study subject identifier(s), date of specimen collection, lab name, and date of printout. • Hard copy lab report from research/ commercial (send-out) lab with appropriate study subject identifier(s) and date of specimen collection, or • Hard copy of correspondence (e.g., e-mail from Data Manager) that study subject has reached a study-defined lab-based endpoint.	• For study-defined clinical or laboratory endpoints, the study subject's SD must document the specifics of the event(s)/test(s) as required by the Protocol, and/or an endpoint-specific CRF. Results of all diagnostic evaluations needed to substantiate the diagnosis must be included in the study subject's SD records. • Lab or diagnostic reports must have an official header or letterhead identifying where the test was performed. • Lab printouts ("print screens") retrieved from an institution's computer system are considered official representations of the source document as long as the institution lab name is part of the print off, the subject's name or study PID or patient identifier, date of test, and date of printout are included. If the lab printout does not include the institution laboratory name and date of printout, the site must document this information on the printout, and initial and date their entry.
Entry Criteria See also Contraception, current method of birth control, Protocol-required counseling; Exemptions, from entry criteria; Medical History and/or Physical Exam, general; Urinalysis, Urine Pregnancy Testing; and Deviations from Protocol.	**Required (one of the following):** • Chart Note, or • Eligibility Checklist (the checklist used for study subject randomization) corresponding to correct Protocol version	For Protocol-specific entry criteria, a Chart Note or completed Eligibility Checklist that addresses each specific criterion must be present in the SD. The note or checklist must be signed, credentialed, and dated by the clinician responsible for enrolling the study subject. **Pertinent negatives**: Exclusion criteria may require that the study subject not be using any of a long list of concomitant medications, or not have any of a list of diseases. For each group of exclusion criteria, it is sufficient to include a note in the study subject's chart such as: "None of the concomitant medications excluded by the Protocol are being used by the study subject." As an alternative, sites may address the excluded groups of medications and/or diseases in their Eligibility Checklist. However, a blanket statement regarding all such exclusion criteria, such as "The study subject does not meet any of the exclusion criteria outlined in the Protocol," will be considered inadequate.
Error Corrections	**Required:** Error corrections to SD must be made by crossing out the incorrect entry with a single line, without obliterating the original entry. The correction is then inserted, and the change is initialed and dated by the person making the change. The use of white-out is never acceptable.	Error corrections that obliterate original entries, that are not initialed and dated, or that make use of white-out, are unacceptable, and may be deemed inadequate source documentation.

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Exemptions, from entry criteria See also Entry Criteria and Deviations from Protocol.	DMID does not allow exemptions from entry criteria.	
Flowsheets	**Optional:** • Pharmacokinetic flowsheets • Vital signs flowsheets • Weight/anthropometric measurements	**Required, if used as SD:** Flowsheets intended to be used as SD must be initialed (preferably signed) and dated by the clinician responsible for flowsheet entries. If a flowsheet is used only to record observations that are summarized elsewhere in the SD (e.g., in a Chart Note), no initialing is required. If the use of a flowsheet extends from one care provider to another, or over multiple time periods (e.g., shifts or days), the flowsheet must be initialed and dated at each sequential time point when an entry is made by a different care provider, or at the beginning of the next time period, whichever occurs first. Flowsheet entries made for timed serial evaluations (e.g., vital signs, pharmacokinetics) that occur over an extended period, yet are recorded by the same care provider, do not require separate initialing. However, individual entries must be timed and dated.
Forms, study subject completed	See Questionnaires, study subject completed.	
Hematology	See Lab tests, Routine, specimen collection and results.	
Inadequate Source Documentation	**Required:** All available source documentation for Protocol-required data must be provided to the monitor at the time a study subject's CRF notebook is reviewed. It is neither the monitor's responsibility to search for source documents, or to travel to another site to obtain access to SD. When an occasional source document is not in the research record (such as a missing lab slip or a document that is temporarily in another department of the hospital), the monitor will ask the site staff to provide the document as soon as possible, during the course of the site visit. The record will not be cited for Inadequate Source Documentation if the missing document is provided to the monitor for review before the completion of the site visit, and it is found to be adequate. As per standard FDA auditing practices, research records (consent forms, source documents, CRFs, etc.) must be inspected on-site by the monitor. It is unacceptable for study personnel to submit missing SD to a monitor BETWEEN site visits, unless they have been specifically instructed to do so by DMID.	

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	Training Point The DMID monitor is responsible for evaluating the adequacy of SD according to Good Clinical Practice (GCP) standards. The overall principle concerning completeness is that, if SD is comprehensive and complete, one should be able to use the SD to reproduce all of a study subject's study data in the event that the CRFs are lost or destroyed. The overall principle concerning accuracy is that, if SD is factual, it should be internally consistent as well as verifiable against external medical documentation. Legal and ethical principles that pertain to medical documentation also apply to SD. See also Documentation Standards. If a CRF used in a particular study requires information that is neither explicitly nor implicitly required by the Protocol, and SD to support such information is inadequate or missing, it will not be counted as Inadequate Source Documentation. However, the monitor will report the finding to their Clinical Project Manager, who will determine the need to obtain further clarification from DMID.	
Informed Consent See also Informed Consent requirements prior to study enrollment.	**Required:** Informed consent documents must be signed and dated in ink by the study subject, parent/guardian, or legally authorized representative. The consent must be signed/dated before Protocol screening commences. The consent document used must be the IRB-approved version corresponding to the Protocol version approved by the IRB that was current when the screening was initiated. If a study subject, parent/guardian or legally authorized representative is unable to read (illiterate), an impartial witness must be present during the entire informed consent discussion. The written informed consent document and any other written information to be provided to the subjects must be read to and explained to the subject, the parent/guardian or the subject's legally authorized representative. After being given the opportunity to ask questions, the subject or the subject's legally acceptable representative must sign and personally date the consent form. By signing the Informed Consent form, the witness attests that the information in the consent form and any other written information was accurately explained to the subject or the subject's legally acceptable representative, and that the informed consent was freely given by the subject or the subject's legally acceptable representative.	The following criteria from DMID will be applied to evaluate Consent Forms for reportable deviations: • Study subject's (or parent/guardian's) signature is not on the consent; • Study subject's (or parent/guardian's) signature is not dated; • Study subject's (or parent/guardian's) signature is dated after the initiation of Protocol screening;[1] • An incorrect version of the Consent Form is used, compared to the Protocol/consent approved by the IRB at a given time; • Initials of subject are used instead of a signature; • Signature and date are not in permanent ink; • Study subject's (or parent/guardian's) signature is fabricated or falsified; • Informed Consent Form cannot be found during a monitoring visit. • No documentation on CRF or SD stating that consent was obtained prior to initiation of screening/study procedures.

[1] If a site customarily uses IRB-approved screening consents for all study subjects, or for all study subjects screened for certain Protocols, the screening consent must be signed/dated before Protocol screening AND the Protocol consent must be signed/dated before randomization.

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	The subject or the subject's representative may sign with a personal mark rather then name. Other culturally accepted identifying indicators, such as thumbprint, may be substituted but these must be reviewed and approved on a case by case study basis with DMID regulatory. When a mark or other indicator is used a witness' signature must be obtained, to attest to the identity of the person making the mark. The informed consent document must be provided in a language understandable to the prospective subject or the subject's legally authorized representative. Translations should be made for non-English speaking subjects. In cases where there is a subject for whom a translated consent document is not available, the short form method described above may be used with the assistance of a qualified translator. **Training Point** The Code of Federal Regulations, 45 CFR 46 and ICH E6, requires study subjects or their guardians to sign an informed consent document before participating in an investigational study. Study subjects participating in DMID clinical trials (or their parents/guardians) must sign and date an Informed Consent for all DMID clinical studies in which the study subject is enrolled. (Local IRBs may have additional requirements, e.g., the signature of a witness, translator, or Principal Investigator.) The methods of providing and documenting informed consent for non-literate populations are addressed in The Code of Federal Regulations (45CFR46.117; 21CFR50.27 (b) (2) and FDA Guidance E6 (ICH) GCP section 4.8.9. DMID will need to review the appropriateness of the procedures per study prior to initiation. It is acceptable for sites to maintain Consents in a file separate from a study subject's SD file, provided the site does this consistently for all study subjects enrolled in the study, and maintains any updated versions of the signed Consents in the same manner.	The following criteria from DMID will be applied for reportable deviations to evaluate Consent Forms for subject or the subject's legally acceptable representatives who are unable to read (illiterate): • Impartial witness signature is not on the consent; • Impartial witness signature is not dated; • Impartial witness signature is dated after the initiation of Protocol screening; • An incorrect version of the Consent Form is used, compared to the Protocol/consent approved by the IRB at a given time; • Impartial witness initials are used instead of a signature; • Signature and date are not in permanent ink; • Impartial witness signature is fabricated or falsified; • Informed Consent Form cannot be found during a monitoring visit; • No documentation on CRF or SD stating that consent was obtained prior to initiation of screening/study procedures

Topic	Source Documentation Methods/Procedures	Adequacy Criteria
Informed Consent requirements prior to study enrollment	**Training Point** The FDA IRB and Clinical Investigation Information Sheets[2] issued in October 1995 provide guidance concerning informed consent requirements in relation to the timing of research-specific screening tests: "...While an investigator may discuss availability of studies and the possibility of entry into a study with a prospective study subject without first obtaining consent, informed consent must be obtained prior to initiation of any screening procedures that are performed solely for the purpose of determining eligibility for research" "Procedures that are to be performed as part of the practice of medicine and which would be done whether or not study entry was contemplated, such as for diagnosis or treatment of a disease or medical condition, may be performed, and the results subsequently used for determining eligibility, without first obtaining consent. On the other hand, informed consent must be obtained prior to initiation of any screening procedures that are performed solely for the purpose of determining eligibility for research. "	
Initials, use of	**Optional:** • Signature sheet, maintained in Protocol-specific Regulatory File	Initials can be used in place of research clinicians' or other personnel's signatures, provided that a signature key, inclusive of the following, is maintained in the Protocol-specific Regulatory File: signature, credentials (if applicable), and corresponding handwritten initials.
Lab tests, Research, specimen collection and results See Case Report Forms, used as Source Documentation. See Endpoints, clinical or laboratory (if required by Protocol) and Electronic Medical Records.	**Recommended for Specimen Collection (one of the following):** • Chart Note, or • Flowsheet entry • CRF used as SD **Required for Results, if available (one of the following):** • Hard-copy lab report with appropriate study subject identifier(s) and date of specimen collection, or • "Print Screen" copy of electronic lab report with appropriate study subject identifiers, lab name, date of printout and date of specimen collection NOTE: For batched and/or blinded research lab analyses, no documentation of results is required in the study subject's SD unless the unblinded results were disclosed to the site for the purposes of study subject management, study termination, or re-randomization/step assignment.	**Regarding Documenting Specimen Collection:** Maintaining documentation that Protocol specimens were drawn and dispatched appropriately is consistent with GCP. Chart Notes/flowsheet entries should be signed and dated to document that particular specimens were drawn and dispatched per Protocol requirements. However, if only a hard-copy "print screen" **lab report** is available for review, the monitor will not cite *Inadequate Source Documentation* as long as the report contains appropriate study subject identifiers and the date of specimen collection. Lab reports must have an official header or letterhead identifying where the test was performed and lab reports must contain a study subject identifier. Lab printouts ("print screens") retrieved from an institution's computer system are considered official representations of the source document as long as the institution lab name is part of the printout, the subject's name, study PID or patient identifier, date of test, and date of printout are included. If the lab printout does not include the institution laboratory name and date of printout, the site must document this information on the printout, and initial and date their entry.

[2] FDA Information Sheet, "Screening Tests Prior to Study Enrollment," Food and Drug Administration, October 1995.

Topic	Source Documentation Methods/Procedures	Adequacy Criteria
Lab tests, Routine, specimen collection and results See Toxicities and Electronic Medical Records.	**Recommended for Specimen Collection (one of the following):** • Chart Note, • Flowsheet entry, or • CRF used as SD **Required for Results (one of the following):** • Hard-copy lab report with appropriate study subject identifier(s) and date of specimen collection, or • "Print Screen" copy of electronic lab report with appropriate study subject identifiers, lab name, date of printout, and date of specimen collection	**Regarding Documenting Specimen Collection:** Maintaining documentation that Protocol specimens were drawn and dispatched appropriately is consistent with GCP. Chart Notes/flowsheet entries should be signed and dated to document that particular specimens were drawn and dispatched per Protocol requirements. However, if only a hard copy or "print screen" **lab report** is available for review, the monitor will not cite *Inadequate Source Documentation* as long as the report contains appropriate study subject identifiers and the date of specimen collection. Lab reports must have an official header or letterhead identifying where the test was performed and lab reports must contain a study subject identifier. Lab printouts ("print screens") retrieved from an institution's computer system are considered official representations of the source document as long as the institution lab name is part of the print off, the subject's name (or study PID or patient identifier), date of test, and date of printout are included. If the lab printout does not include the institution laboratory name and date of printout, the site must document this information on the printout, and initial and date their entry.
Medical History and/or Physical Exam, general	**Required per Protocol (one or more of the following):** • Chart Note, • History and Physical Exam form, • CRF used as SD, • Consult Notes, • Hard-copy lab report with appropriate study subject identifier(s) and date of specimen collection, and/or • "Print Screen" copy of electronic lab report with appropriate study subject identifier(s) and date of specimen collection	Medical History and/or Physical Examination Documentation if Protocol-required: • A documented verbal history from the subject may be acceptable based on Protocol. • If medical history is documented by study subject, it must be reviewed and signed, dated, and credentialed by clinician. • Physical exam must be completed and signed, dated, and credentialed by clinician. Other requirements will depend on specific history required per Protocol.
Microbiology	See requirements under Lab tests, Routine or Lab tests, Research.	
Neurological Exams	**Examples:** • EEG, interpretative consult note • EMG, interpretative consult note • Peripheral neuropathy, detailed CRF-directed assessment	See criteria for Chart Note, clinician; Consult Notes; or Case Report Forms, use as Source Documentation.

Topic	Source Documentation Methods/Procedures	Adequacy Criteria
Neuropsychological Exams	**Required (one of the following):** • Chart Note, or • Detailed CRF-directed assessment	See criteria for Chart Note, clinician; Consult Notes; or Case Report Forms, use as Source Documentation.
Progress Notes, clinician	See Chart Note, clinician.	
Quality of Life (QOL), study subject reported	See Questionnaires, study subject completed.	
Questionnaires, study subject completed	**Required per Protocol (one of the following):** Document that study subject completed the form per Protocol evaluation schedule. This can be accomplished by: • Entering a note into the study subject's chart or CRF used as SD indicating the specific form which was completed on a specified date; or, • Indicating on a checklist the study subject-completed form which was completed on a specified date; or, • Including in the SD a copy of the study subject-completed form that is signed/dated in the margin by study personnel. **Training Point** Data on study subject-completed CRFs (Health Status or QOL questionnaire) are considered study subjective and do not require SD.	
Radiology, diagnostic	**Required (one of the following):** • X-ray, CT scan, MRI interpretative consult note or computer printout, signed, credentialed, and dated by responsible radiologist • Non-radiologist clinician's interpretation note (e.g., for a routine chest X-ray), signed, credentialed, and dated by responsible clinician	Consult notes must include appropriate study subject identifier(s) and be signed and dated by the clinician responsible for the note. See also Consult Notes.
Research Record	**Training Point** All documents corresponding to a given study subject's participation in a clinical investigation constitute a research record. These consist of the study subject's signed Informed Consent, source documentation (case history), study prescriptions, investigational pharmacy records, and Case Report Forms (CRF). A Clinical Site Monitor conducting "record review" may request to inspect any or all of the above types of documents. Investigators are responsible for maintaining accurate and complete research records (referred to as "case histories" in FDA regulations). Sites must be able to produce any research record in its entirety in the event of an FDA inspection.	
Serology	See requirements under Lab tests, Routine or Lab tests, Research.	

Topic	Source Documentation Methods/Procedures	Adequacy Criteria
Shadow Files See also: Certified: Copies Documentation Standards Research Records	Shadow files are certified copies of the study subject's original laboratory reports, medical record, or clinic chart. These files, consisting of copied source documents, are intended to reflect a subject's complete, study specific record. Shadow files may be useful in settings such as: where the participant is still in in-patient care and the medical record is not available; where records are coming from multiple institutions; to establish a complete study file when a source workbook or CRFs are not provided for treatment trials for remote data entry; or in vaccine studies where additional information from the medical record is required for adverse events. Examples of sections of the medical record that might be included in a shadow file: • Documentation of the consent process • Screening results • Baseline events, including medical history and physical exam • Vital status • Clinical and laboratory findings • Management of study drugs/agents and toxicities • Concommitant medications Monitors and FDA auditors may request to see the original documents to verify validity of data for trial related monitoring or to look for unreported adverse events. If the site is not able to produce original source documents or certified copies during a monitoring review, the data will be considered as having inadequate source documentation. **Training Point:** Original records are ideal but shadow files are acceptable. Monitors may occasionally request to see the original documents during routine monitoring to verify their existence-it does not mean that alterations or fraud is suspected. Hospital records used to substantiate data must meet institutional policy and will not be monitored for adherence to the GCP standards that research-specific records are required to follow.	
Signs/Symptoms, clinician observed	See Chart Note, clinician; Flowsheets; and Toxicities.	
Signs/Symptoms, study subject reported	See Questionnaires, study subject completed; and Toxicities.	
Storage, of source documents	**Training Point** Source documents must be maintained at the site. If SD are archived, it is the site's responsibility to retrieve and organize all source documents for the clinical site monitoring visit.	
Study subject Identifiers	See Confidentiality, study subject	
Subject Specific Information	Contains personal information such as name, contact information, birth date, hospital record numbers, information needed for compensation, and PID. This document is not a Case Report Form and is linked to it only by the PID. Subject Specific Information belongs to the site. The monitor should have access to this document if requested.	

Topic	Source Documentation Methods/Procedures	Adequacy Criteria
Toxicities, reviewing of (adverse events, signs and symptoms, or abnormal lab results)	**Required (one of the following):** • Chart Note, • Flowsheet, • Adverse Event/Symptom Checklist, • CRF used as SD, or • Annotated lab slip, signed and dated by responsible clinician	All reviewed adverse events, and/or signs and symptoms must be documented in the CRF or in additional SD. For lab values outside normal range, clinical significance must be documented by responsible clinician; this may be documented in the CRF, additional SD, or annotated lab slip. For Protocol-reportable and serious adverse events, sites must note in the CRF/SD the clinician's opinion regarding relationship of the event to study medication(s).
Urinalysis, Urine Pregnancy Testing Also see Lab tests, routine, specimen collection and results.	**Required for CLIA Waived urine dipsticks and urine pregnancy tests performed by site:** Document test results including when the test was done, the test results, and who performed or interpreted the results in: • Log format, • CRF used as SD, or • Chart Note **Recommended for CLIA Waived urine pregnancy tests performed by site:** • Document in SD the date of the last menses.	Documentation of CLIA Waived urine dipstick and urine pregnancy tests performed by the site must contain the following information: when the test was done; the test results; and who performed or interpreted the results. A urine pregnancy log can serve as your source documentation. For urinalysis and pregnancy tests sent to CLIA-certified labs, SD methods/procedures and adequacy criteria for lab tests, routine are to be followed. Note: Urine pregnancy (not serum) and dipstick urinalysis is eligible for CLIA waiver. www.cms.gov provides information on waivers
Virology	See requirements under Lab tests, Routine or Lab tests, Research.	
Vital Signs	**Required per Protocol (one of the following):** • Chart Note, • Flowsheet, or • CRF used as SD	See criteria for Chart Note, clinician; Flowsheets; and Case Report Forms, used as Source Documentation.
Weight/Height	**Required per Protocol (one of the following):** • Chart Note, or • Flowsheet, or • CRF used as SD	See criteria for Chart Note, clinician; Flowsheets; and Case Report Forms, used as Source Documentation.